Improving Suspicious Breast Lesion Characterization Using Lesion Fractional Volume Washout Kinetic Analysis

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Introduction: Dynamic contrast-enhanced (DCE) breast MRI has been shown to be very sensitive in cancer detection [1,2]. Most malignant tumors demonstrate an initial enhancement followed by a rapid wash-out (WO) or plateau curve in the post-contrast signal intensity time courses. The WO curve mainly reflects the hypervascularity associated with tumor angiogenesis essential for tumor growth [3-5]. Although most benign lesions exhibit a slower but persistent enhancement without the WO behavior [1], false-positive kinetic curves were frequently observed in many benign lesions including fibroadenomas, proliferative fibrocystic changes, atypical ductal hyperplasia, etc. [6,7]. This results in a low specificity and consequently a smaller positive predictive value (PPV) for biopsies. In a recent study involving a total of 125 suspicious or highly suggestive of malignant lesions (BI-RADS 4 or 5), the biopsies resulted in 42 malignant tumors and 83 benign lesions, showing a 33.6% PPV at the clinic [8]. Our recent preliminary study demonstrates the potential of using WO volume fraction as a new biomarker for differentiating benign from malignant contrast-enhancing breast lesions [9]. The hypothesis is that WO volume fraction, those voxels showing rapid wash-in and wash-out behavior in proportion to total lesion voxels showing rapid wash-in, has the potential to be a biomarker for indicating the degree of hypervascularity associated with tumor angiogenesis. Currently, the usual clinical approach is based on selecting only the most suspicious voxels within a lesion to characterize that lesion and does not incorporate the proportion of the most suspicious wash-out voxels to the total lesion volume. We hypothesized that the WO volume fraction for benign proliferation might be relatively small in comparison to malignant lesions, considering that an aggressive cancer cell growth is most likely accompanied by relatively larger angiogenesis [9]. In this study we investigated using the WO volume fraction as a biomarker for improving the characterization of suspicious contrast-enhancing breast lesions, aiming to improve the PPV of biopsies and consequently to reduce the number of unnecessary biopsies.

Methods and Materials: Over 650 standard clinical breast MRI examinations since 2007 from our clinic were retrospectively reviewed. Study lesions were mass like enhancement larger than 5 mm, were initially detected on breast MRI and were assigned a BI-RADS assessment of 4 (suspicious abnormality) or 5 (highly suggestive of malignancy), resulting in a total of 43 suspicious lesions. Lesions with BI-RADS assessment of 6 (known biopsy-proven malignancy) were not included in this study. The study excluded those lesions with BI-RADS assessment of 4 or 5 that did not go on to biopsy or their histopathology reports could not obtained (15 lesions in total out of the 43 suspicious lesions). A total of 28 suspicious contrast-enhanced lesions (25 lesions with BI-RADS assessment of 4 and 3 lesions with BI-RADS assessment of 5) in 27 patients had subsequent biopsy with available histopathology reports and comprised the lesion set for this study. The MRI examinations were acquired on a GE clinical 1.5T scanner using a standard clinical protocol for breast DCE-MRI [9]. Post-contrast imaging included five phases with a scan time of 90s for each phase. All lesions were identified by a board-certified experienced breast MRI diagnostic radiologist. For each lesion, the boundary of the contrast-enhanced lesion on the first phase post-contrast images was semi-automatically determined using an in-house developed Matlab-based software algorithm which utilizes the MRI signal intensity difference between the contrast-enhanced lesion and its surrounding tissues, resulting in an objective region of interest (ROI) of the lesion (Fig. 1, left) [9]. The determined lesion boundaries on each slice were confirmed by the radiologist. A linear least squares fitting of the post-contrast signal intensity time course was performed and then the slope of the fitted line was computed pixel-by-pixel; a negative slope indicated a WO curve (Fig. 1, right). The total volume for a lesion and the total volume of WO voxels within the lesion were computed, and the ratio of the latter to the former was further calculated to yield the WO volume fraction for the lesion. The lesion boundary determinations and the WO volume fraction computations were blinded to the histopathology reports.

Results and Discussion: The biopsies resulted in ten malignant tumors (MT) (the three highly suggestive of malignant lesions with BI-RADS assessment of 5 and seven lesions with BI-RADS assessment of 4) and eighteen benign lesions (BL) (Fig. 2), yielding a 35.7% PPV of the biopsies. The MT include 7 infiltrating ductal carcinoma and/or DCIS and 3 invasive lobular carcinoma. The BL include fibrocystic changes, fibrosis, and fibroadenoma. For the BL, the mean and standard deviation of the WO volume fraction was 21.8±19.0 (%), ranged from 2.2% to 64.7%. For the MT, however, the WO volume fraction was 45.3±14.6 (%) with the range from 26.5% to 68.1%, significantly larger than that for the BL ($p<0.001$) (Fig. 3). This significantly larger WO volume fraction for the MT was most likely produced by the hypervascularity associated with tumor angiogenesis, but the smaller WO volume fraction for the BL mainly reflected a relatively small amount of increased vascularity associated with benign fibrocystic changes and fibroadenoma. These results can be used to improve the characterization of suspicious contrast-enhancing breast lesions. If we choose 25% as a WO volume fraction threshold for characterizing these lesions (see dash-line in Fig. 2), i.e., a WO volume fraction larger than the threshold would be characterized as malignant and a WO volume fraction smaller than the threshold would be characterized as benign, respectively, then all of the MT would be identified as malignant, maintaining the same sensitivity. However, thirteen out of the eighteen BL would be identified as benign, resulting in an 86.8% improvement rate to the PPV of the biopsies (from 35.7% to 66.7%). Accordingly, the total number of unnecessary biopsies would be reduced from 18 to 5, a 72.2% reduction rate. In conclusion, the WO volume fraction was significantly different between the BL and the MT of all the suspicious breast lesions with BI-RADS assessment of 4 or 5. If the WO volume fraction biomarker is confirmed in a large clinical trial, this has the potential to improve the computer-based assessment in breast MRI, greatly increasing the PPV and consequently to greatly reduce the number of unnecessary biopsies.

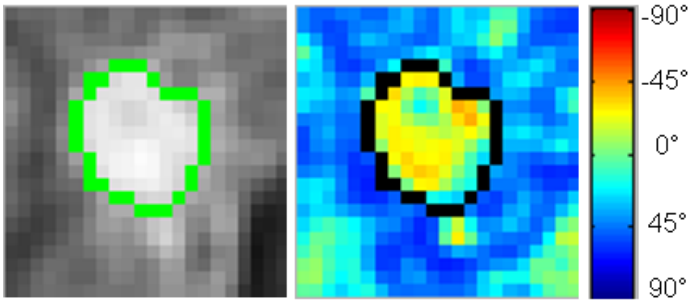

Fig. 1 Left: Illustration of a lesion based on the first post-contrast image. Right: Corresponding image of the color-coded degree of slope for the DCE period. A negative degree indicates a WO curve.

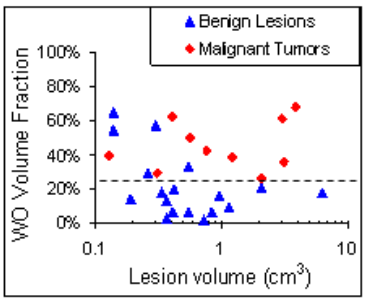

Fig. 2 Distribution of WO volume fraction versus lesion size. The dash-line indicates the 25% threshold value.

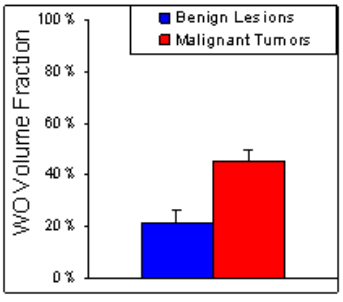

Fig. 3 Comparison of WO volume fraction between the MT and the BL. The error bar denotes the standard error of the mean.

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